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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/701,536	06/18/2001	Gwong-Jen J. Chang	6395-64907-01	5492

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EXAMINER	
PARKIN, JEFFREY S	
ART UNIT	**PAPER NUMBER**
1648	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/22/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/701,536	CHANG, GWONG-JEN J.	
	Examiner	Art Unit	
	Jeffrey S. Parkin, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *03* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 September 2007 and 28 December 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *35-54 and 69* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *35-54 and 69* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f)..

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Office Action

Status of the Claims

Acknowledgement is hereby made of receipt and entry of the communications filed 18 September and 28 December, 2006. Claims 35-54 and 69 are pending in the instant application.

35 U.S.C. § 103(a)

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 35-37, 39-45, 47-49, 51, and 69 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Phillpotts *et al.* (1996) in view of Kozak (1987). The claims are directed toward a nucleic acid comprising a transcriptional unit (TU) that encodes a flavivirus antigen. The claims stipulate that the TU must comprise a prM signal sequence and a ribosomal binding sequence (e.g., GCCGCCGCC). Additional claim limitations specify the flavivirus of interest (e.g., dengue, yellow fever, Japanese encephalitis), antigen(s) encoded by the TU (e.g., prM/M, E, both prM/M and E), promoter selection (e.g., CMV IE), and termination sequences.

As previously set forth, Phillpotts and colleagues provide isolated nucleic acids comprising a transcriptional unit expressing a flavivirus immunogen (see Abstract, p. 743). The transcriptional

unit comprises the St. Louis Encephalitis virus (SLE) prM/E gene (which includes the prM signal sequence). This unit also includes the cytomegalovirus (CMV) major immediate-early (IE) promoter and poly(A) terminator (see second paragraph, p. 744). Compositions comprising the nucleic acid and a pharmaceutically acceptable carrier, as well as, cells comprising the nucleic acids are provided (see third and fourth paragraphs, p. 744). The only limitation of this teaching is that is does not disclose the utilization of a Kozak consensus sequence to facilitate translation. However, Kozak compared the translational initiation sequences of several hundred higher eukaryotes and ascertained the optimal sequences for translational initiation. Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to include a Kozak translational consensus sequence, as taught by Kozak (1987), in the transcriptional unit of Phillpotts *et al.* (1996), since this would facilitate optimum expression of the flavivirus immunogen of interest. Thus, both the motivation and a reasonable expectation of success were present in the prior art.

Response to Arguments

Applicants traverse and submit that nothing in the Kozak teaching references a viral transcription unit comprising the claimed ribosomal initiation sequence and accordingly there is no motivation to combine the teachings relied upon. The examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 U.S.P.Q.2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 U.S.P.Q.2d 1941 (Fed. Cir. 1992).

In this case sufficient motivation to combine the references is clearly provided by Kozak (1987). Kozak unambiguously discloses the optimal sequence for ribosomal initiation in eukaryotic/mammalian cells. The optimal initiation sequence comprises GCCGCCGCCAUGG. This is the exact same sequence employed by applicants in their construct. One of ordinary skill in the art would have had more than sufficient motivation to include this consensus sequence in the TU of Phillpotts *et al.* (1996) since the inclusion of this sequence in the TU would reasonably be expected to lead to improved translational efficiency. Thus, both a reasonable expectation of success and the motivation to arrive at the claimed invention were present in the prior art.

Applicants additionally argue that the examiner employed improper hindsight reasoning to arrive at the claimed invention. It must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 U.S.P.Q. 209 (C.C.P.A. 1971).

Finally, applicants contend that the claimed invention provides unexpectedly superior results since none of the claimed constructs elicit high titer neutralizing antibodies after a single inoculation. Applicants are reminded that none of these limitations appear in the claims. The claims are simply directed toward nucleic acids comprising the recited transcriptional unit. However, the purportedly unexpected results are consistent with the teachings of Phillpotts *et al.* (1996). This teaching clearly demonstrates that "Significant protection was achieved against SLE virus by a single im injection of 50ug pSLE1 in comparison to

control groups" (see p. 745). Thus, this construct is clearly capable of inducing protective immune responses against flaviviruses.

Claims 38, 46, and 50 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Phillpotts *et al.* (1996) in view of Kozak (1987), as set forth *supra* in claims 35-37, 39-45, 47-49, 51, as evidenced by Konishi *et al.* (1992). The aforementioned references do not demonstrate that prM/E expression results in the production of subviral particles comprising both proteins. However, Konishi and colleagues clearly demonstrate that coexpression of the prM/E genes of Japanese encephalitis virus (JEV) results in the production of subviral particles comprising both proteins (see Abstract, p. 714; Results, pp. 716-717). It was also demonstrated that said particles were highly immunogenic. Therefore, one of ordinary skill in the art would have reasonably expected coexpression of the prM/E genes to produce highly immunogenic subviral particles. Applicant's arguments have been addressed in the preceding paragraphs.

35 U.S.C. § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 69 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Two separate requirements are set forth under this statute: (1) the claims must set forth the subject matter that applicants regard as their invention; and (2) the claims must

particularly point out and distinctly define the metes and bounds of the subject matter that will be protected by the patent grant. The claim references nucleotides 16 to 28 of SEQ ID NO.: 5. This sequence references an amino acid sequence and fails to contain the recited nucleotides. Appropriate correction is required.

Finality of Office Action

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a). A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. § 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Correspondence

Any inquiry concerning this communication should be directed to Jeffrey S. Parkin, Ph.D., whose telephone number is (571) 272-0908. The examiner can normally be reached Monday through Thursday from 10:30 AM to 9:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Bruce R. Campell, Ph.D., can be reached at (571) 272-0974. Direct general status inquiries to the Technology Center 1600 receptionist at (571) 272-1600. Informal communications may be submitted to the Examiner's RightFAX account at (571) 273-0908.

Applicants are reminded that the United States Patent and Trademark Office (Office) requires most patent related correspondence to be: a) faxed to the Central FAX number (571-273-8300) (updated as of July 15, 2005), b) hand carried or delivered to the Customer Service Window (now located at the Randolph Building, 401 Dulany Street, Alexandria, VA 22314), c) mailed to the mailing address set forth in 37 C.F.R. § 1.1 (e.g., P.O. Box 1450, Alexandria, VA 22313-1450), or d) transmitted to the Office using the Office's Electronic Filing System. This notice replaces all prior Office notices specifying a specific fax number or hand carry address for certain patent related correspondence. For further information refer to the Updated Notice of Centralized Delivery and Facsimile Transmission Policy for Patent Related Correspondence, and Exceptions Thereto, 1292 Off. Gaz. Pat. Office 186 (March 29, 2005).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,

Jeffrey S. Parkin, Ph.D.
Primary Examiner
Art Unit 1648

18 March, 2007